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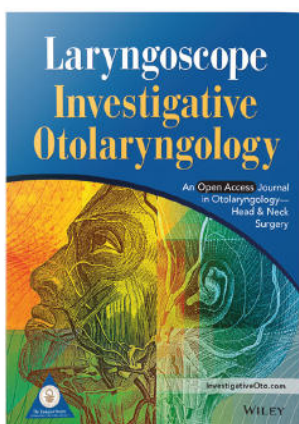


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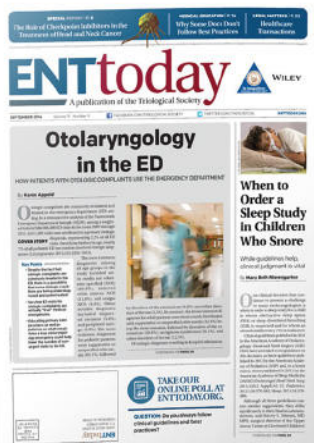


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# Cricotracheal Resection for Adult Subglottic Stenosis: Factors Predicting Treatment Failure

Ashok R. Jethwa, MD ; Wael Hasan, MBBCh, MCh; Carsten E. Palme, MD; Antti A. Mäkitie, MD, PhD; Osvaldo Espin-Garcia; David P. Goldstein, MD, MSc ; Ralph W. Gilbert, MD; Shaf Keshavjee, MD, MSc; Andrew Pierre, MD, MSc; Patrick J. Gullane, MB

**Objectives/Hypothesis:** Identify predictors of decannulation failure after cricotracheal resection (CTR) and thyrotracheal anastomosis (TTA) in patients with subglottic stenosis (SGS).

**Study Design:** Retrospective cohort study.

**Methods:** Charts of patients undergoing CTR and TTA for SGS at the University Health Network, Toronto, Ontario, Canada between 1988 and 2017 were reviewed. Patient, pathology, treatment, and outcome data were collected. The end points for statistical analysis were development of restenosis and permanent tracheostomy.

**Results:** One hundred fourteen patients (n = 114) were eligible for inclusion in this review. The mean age at primary resection was 46.9 years, 95 (83%) were females, and 19 (17%) were males. The rate of restenosis and permanent tracheostomy was 13% and 5%, respectively. Sixty-two patients (54%) underwent a CTR and TTA, and 52 patients (46%) underwent a CTR, laryngofissure, and TTA. Traumatic stenosis (odds ratio [OR] = 10.3,  $P = .017$ ), longer T-tube duration (OR = 1.2,  $P = .011$ ), combined glottic/subglottic stenosis (OR = 10.47,  $P = .010$ ), start of the stenosis at the vocal cords (OR = 6.6,  $P = .029$ ), postoperative minor complications (OR = 13.6,  $P = .028$ ), and need for repeat surgery (OR = 44.1,  $P < .001$ ) were associated with an increased risk of requiring permanent tracheostomy.

**Conclusions:** CTR and TTA are excellent surgical approaches for adult patients with subglottic stenosis. In this study, 5% of patients required permanent tracheostomy. Factors predicting treatment failure include traumatic stenosis, longer T-tube duration, combined glottic/subglottic stenosis, start of stenosis at the level of vocal cords, postoperative minor complications, and need for repeat surgery.

**Key Words:** Adult subglottic stenosis, cricotracheal resection, prognostic factors.

**Level of Evidence:** 4

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## INTRODUCTION

Subglottic stenosis is a potentially life-threatening condition. It is generally classified into congenital and acquired etiologies. Laryngeal trauma and iatrogenic injuries, typically during intubation, are the most common underlying etiology for adult subglottic stenosis.<sup>1</sup> External trauma, which can be either blunt or penetrating, is less often implicated in the etiology of airway stenosis. In the remainder of patients, the exact etiology is idiopathic in nature.<sup>2</sup> The

subglottis and the posterior glottis are the two most commonly involved sites.<sup>3</sup>

The management of airway stenosis presents a major therapeutic challenge. Treatment options vary depending on the underlying etiology, severity of the condition, comorbidities, as well as patient's wishes and expectations. Management of airway stenosis is aimed at restoring all forms of function leading to normal ventilation, speech, and swallow. Many techniques have been described. These can be broadly divided into endoscopic and external techniques. The goal of these procedures is to maximize the airway's volume and to maintain this during the healing phase. Dilatation, stenting, and surgical resection using both endoscopic and external techniques have been used.<sup>4</sup> The outcome of the majority of the endoscopic techniques is temporary. A permanent resolution will often require a more complex open procedure during which the stenotic segment is resected and reconstructed to maintain a functional, uncompromised airway.

There are limited data investigating predictors of restenosis and decannulation failure in patients after cricotracheal resection (CTR). Airway comorbidities (asthma, chronic obstructive pulmonary disease [COPD], unilateral vocal cord paralysis), postoperative complications, and length of resection have previously been reported as risk factors for

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TABLE I. Patients' Characteristics (N = 114).	
Covariate	Value
Sex	
Female	95 (83)
Male	19 (17)
Age at surgery, yr	
Mean (SD)	46.9 (13.2)
Median (minimum, maximum)	47.3 (12.4, 80)
Airway	
Stridor	49 (43)
Tracheostomy dependent	28 (25)
Voice	
Dysphonia	20 (18)
Acceptable	94 (82)
Idiopathic	
No	51 (45)
Yes	63 (55)
History of airway trauma	
No	107 (94)
Yes	7 (6)
Comorbidities	
None	80 (70)
Yes	34 (30)
Length of stenosis, cm	
Mean (SD)	2.2 (0.7)
Median (minimum, maximum)	2 (1, 4.5)
Missing	3
Length of resection, cm	
Mean (SD)	2.9 (0.7)
Median (minimum, maximum)	3 (1, 5)
Missing	23
T-tube duration, d	
Mean (SD)	65.1 (140.3)
Median (minimum, maximum)	43 (0, 1,451)
Tracheostomy	
No	66 (58)
Yes	48 (42)
Prior endoscopic surgery	
No	46 (40)
Yes	68 (60)
Prior external surgery	
No	91 (80)
Yes	23 (20)
Diagnosis	
Subglottic	91 (80)
Combined	21 (18)
Tracheal	2 (2)
Grade of stenosis	
≤ 50%	43 (43)
51%–70%	32 (32)
71%–99%	21 (21)
100%	5 (5)

(Continues)

TABLE I. Continued	
Covariate	Value
Missing	13
Start of stenosis	
At vocal cord	17 (15)
Below	96 (85)
Missing	1
Procedure	
CTR, LF, TTA	52 (46)
CTR, TTA	62 (54)
Pathology	
Benign	3 (3)
Fibrosis, chronic inflammation	111 (97)
Complication	
None	78 (68)
Major	16 (14)
Minor	20 (18)
Postoperative airway	
None	14 (12)
T tube	92 (81)
Tracheostomy	8 (7)
Repeat surgery	
No	98 (86)
Yes	16 (14)
Restenosis	
No	99 (87)
Yes	15 (13)
Permanent tracheostomy	
No	108 (95)
Yes	6 (5)

Data are presented as number (%) unless indicated otherwise.  
CTR = cricotracheal resection; LF = laryngofissure; SD = standard deviation; TTA = thyrotracheal anastomosis.

retreatment.<sup>5</sup> In pediatric patients, severity of stenosis, glottic involvement, and comorbidities are predictors of less favorable outcomes.<sup>6</sup>

The objective of the study was to evaluate outcomes and identify predictors of restenosis and decannulation failure in adult patients with subglottic or upper tracheal stenosis managed with CTR or tracheal resection.

## MATERIALS AND METHODS

After institutional research ethics board approval, a retrospective review was conducted of all patients who underwent surgery for subglottic stenosis at the Toronto General Hospital, University Health Network, Toronto, Ontario, Canada from January 1, 1988 to July 1, 2017. Patients with isolated posterior glottic stenosis or malignant pathology were excluded. Patient (gender, age, comorbidities), stenosis (symptoms, previous treatment, site, length, grade), treatment (CTR and thyrotracheal anastomosis [TTA] ± laryngofissure, length resected, histopathology, time with T tube, complications), and outcome data (restenosis rate, salvage surgery, permanent tracheostomy, follow-up) were collected from the electronic patient records. Stenosis information, such as length and

TABLE II.  
Univariable Analysis.

Covariate	Permanent Tracheostomy		Restenosis		Composite Outcome	
	OR (95% CI)	P Value	Global P Value	OR (95% CI)	P Value	Global P Value
Sex			.28			.71
Female	Reference			Reference		
Male	2.68 (0.45–15.79)			1.3 (0.33–5.12)		1.18 (0.3–4.63)
Age at surgery	1.01 (0.95–1.07)	.8		0.98 (0.94–1.02)		0.99 (0.95–1.03)
Airway		.7				.79
None	Reference			Reference		
Stridor	2.35 (0.23–23.53)	.47		1.25 (0.37–4.18)	.72	
Tracheostomy dependent	2.77 (0.24–32.18)	.42		0.49 (0.09–2.75)	.42	.73
Idiopathic	N/A	.99		0.67 (0.23–2)	.47	.32
Trauma	10.3 (1.51–70.26)	.017*		2.89 (0.51–16.47)	.23	2.66 (0.47–15.04)
Comorbidities	N/A	1.0		3.21 (1.06–9.72)	.039*	3.75 (1.27–11.13)
Length	1.91 (0.69–5.31)	.22		0.87 (0.41–1.85)	.71	0.79 (0.37–1.67)
Length resected	1.46 (0.43–4.92)	.55		0.71 (0.32–1.58)	.4	0.68 (0.31–1.48)
Days with T tube	1.2 (1.04–1.38)	.011*		1.08 (0.98–1.19)	.12	1.09 (0.99–1.2)
Preexisting tracheostomy	7.56 (0.85–66.95)	.069		1.24 (0.42–3.68)	.7	1.45 (0.5–4.18)
Prior endoscopic surgery	0.32 (0.06–1.81)	.2		1.02 (0.34–3.08)	.98	0.85 (0.29–2.47)
Prior external surgery	0.78 (0.09–7.04)	.83		3.22 (1.01–10.23)	.048*	2.86 (0.92–8.93)
Diagnosis		.035*			.32	.14
Subglottic	Reference			Reference		
Combined	10.47 (1.77–61.77)	.0095*		2.53 (0.76–8.4)	.13	3.24 (1.02–10.26)
Grade of stenosis		1.0				.098
≤ 50%	Reference			Reference		
51%–70%	N/A	1.0		3.73 (0.88–15.79)	.073	4.44 (1.07–18.39)
71%–100%	N/A	1.0		1.11 (0.17–7.13)	.91	1.11 (0.17–7.13)
Start of stenosis		.029*			.19	.06
Below	Reference			Reference		
At vocal cord	6.64 (1.22–36.22)			2.38 (0.66–8.59)	.087	3.22 (0.95–10.88)
Procedure		.3				.053
CTR, LTP	Reference			Reference		
CTR, LF, LTP	2.5 (0.44–14.23)			2.71 (0.86–8.53)		3.06 (0.99–9.48)
Complication		.076			.0071*	.0022*
Major	11.0 (0.93–129.67)	.057		3.37 (0.72–15.85)	.12	3.37 (0.72–15.85)
Minor	13.59 (1.33–138.73)	.028*		7.86 (2.16–28.57)	.0017*	9.73 (2.72–34.77)
Postoperative airway		.74			.72	.77
Repeat surgery	44.09 (4.71–412.42)	<.001*		95 (18.93–476.66)	<.001*	137.22 (25.02–752.7)

\*Statistically significant.

CI = confidence interval; CTR = cricotracheal resection; LF = laryngofissure; N/A = not applicable; OR = odds ratio; TTA = thyrotracheal anastomosis.

grade of stenosis, were obtained from intraoperative description when available. Our technique of CTR has been previously reported.<sup>1</sup> The area of stenosis was retrospectively graded using the Cotton-Myer classification (grade 1, ≤50%; grade 2, 51%–70%; grade 3, 71%–99%; grade 4, 100%).<sup>7</sup>

Complications were defined as major if they required active operative intervention or were life-threatening. Patients who required further surgery for recurrent airway obstruction were defined as having developed restenosis. Those who required a permanent tracheostomy were deemed to have failed therapy.

Patient factors, stenosis characteristics, and treatment factors potentially predictive for the development of restenosis or the need for a permanent tracheostomy were analyzed using logistic regression. Factors were tested one at a time for significant effects using the Wald statistic, and  $P < .05$  was deemed statistically significant. All analyses were performed using R software version 3.5.2 (The R Foundation for Statistical Computing, Vienna, Austria).

## RESULTS

### *Demographics*

One hundred fourteen patients ( $n = 114$ ) were included in this review. Baseline characteristics are described in Table I. The mean age at primary resection was 46.9 years (standard deviation [SD] = 13.2, median = 47.3 [12.4–80]); 95 patients (83%) were females and 19 patients were males (17%). We included one patient under the age of 18 years (12.4) at time of treatment. The etiology of the stenosis was idiopathic in 63 (55%) and traumatic in seven (6%) patients. Significant comorbidities were present in 34 (30%) patients. These included significant medical disorders ranging from diabetes mellitus, chronic gastrointestinal disease, ischemic heart disease, renal failure, and chronic airway limitation. Twenty-eight (25%) patients were tracheostomy-tube dependent on presentation. Past treatments included tracheostomy in 48 (42%), endoscopic laser resection or dilatation was performed in 68 (60%), and open resection in 23 (20%) patients.

### *Stenosis Characteristics*

All patients underwent thorough preoperative evaluation with autoimmune workup, computed tomography scanning, and an endoscopic examination under general anesthesia. A biopsy was taken for histopathological examination in all cases to exclude either an inflammatory process or malignancy. Patients with autoimmune etiology were not offered CTR. The subglottis was the sole site of stenosis in 91 (80%) patients, two (2%) had upper tracheal stenosis, and combined stenosis (i.e., glottis and subglottis) was reported in 21 (18%) cases. Using the Cotton-Myer staging classification, grade I stenosis was present in 43 (43%) patients, grade II in 32 (32%), grade III in 21 (21%), and grade IV in five (5%) patients. Accurate records of the grade of stenosis were missing in 13 patients. The mean length of stenosis was 2.2 cm (SD = 0.7, median 2 [1–4.5]).

### *Treatment Characteristics*

Sixty-two (54%) patients underwent a CTR and TTA, and 52 (46%) patients underwent a CTR and TTA

with additional laryngofissure as previously described by Pearson and Gullane.<sup>1</sup>

The mean length resected was 2.9 cm (SD = 0.7 cm, median = 3 cm [1–5 cm]). Postoperative airway patency was maintained via a T tube in 92 (81%) and a tracheostomy in eight cases (7%). The mean time with a T tube (TT<sub>time</sub>) was 65.1 days [SD = 140.3 days, median = 43 days [0–1451]]. A permanent tracheostomy was necessary in six (5%) patients.

Major complications occurred in 16 patients (14%), and minor complications in 20 (18%) patients. Restenosis requiring active intervention occurred in 15 patients (13%).

### *Univariable Analysis of Restenosis*

Medical comorbidity (odds ratio [OR] = 3.2,  $P = .039$ ), prior external procedure (OR = 3.2,  $P = .048$ ), postoperative minor complication (OR = 7.9,  $P = .002$ ), and need for repeat surgery (OR = 95.0,  $P < .001$ ) were associated with increased risk of restenosis (Table II).

### *Univariable Analysis of Permanent Tracheostomy*

Traumatic stenosis (OR = 10.3,  $P = .017$ ), longer T-tube duration (OR = 1.2,  $P = .011$ ), combined glottic/subglottic stenosis (OR = 10.47,  $P = .010$ ), start of the stenosis at the vocal cords (OR = 6.6,  $P = .029$ ), postoperative minor complications (OR = 13.6,  $P = .028$ ), and need for repeat surgery (OR = 44.1,  $P < .001$ ) were associated with an increased risk of requiring permanent tracheostomy (Table II).

### *Univariable Analysis of Composite Outcome (Restenosis and Permanent Tracheostomy)*

Medical comorbidity (OR = 3.8,  $P = .017$ ), combined glottic/subglottic stenosis (OR = 3.24,  $P = .046$ ), grade 2 stenosis (OR = 4.4,  $P = .040$ ), postoperative minor complication (OR = 9.7,  $P < .001$ ), and need for repeat surgery (OR = 137.2,  $P < .001$ ) were associated with an increased risk of restenosis and permanent tracheostomy (Table II).

Overall, 108 patients (95%) were successfully decannulated. These patients achieved an excellent result in terms of upper aerodigestive tract function satisfactory for all of their activities of daily living.

## DISCUSSION

The primary goal of management in patients with subglottic stenosis is to reestablish a functional airway. Management options include dilatation, endoscopic laser resection, laryngofissure, laryngotracheoplasty, and CTR ( $\pm$  laryngofissure) with TTA.<sup>8–14</sup> Circumferential resection of the upper airway has been described as early as Ogura and Biller in 1971<sup>9</sup> and Gerwat and Bryce in 1974.<sup>10</sup> The combined thoracic and head and neck surgical approach has allowed refinement of this technique, which today is well accepted as an excellent option for the treatment of both glottic and subglottic stenosis. These successes have been substantiated by contemporary reports from Pearson et al. (1986), Grillo et al. (1992), and Courard et al. (1988).<sup>11–13</sup> Hartley and Cotton



(2000) and Monnier et al. (1993) have also demonstrated the successful application of this technique for the treatment of pediatric subglottic stenosis.<sup>15,16</sup>

The management principles in CTR and TTA include complete resection of the pathology, repair and reconstruction of the airway, maintaining the repair to allow healing, and finally successful decannulation. A number of factors are important and can be conveniently divided into patient, disease, and treatment related. Patient comorbidity plays a major role in determining the ability to heal after surgery. The presence of medical comorbidities in this series was a significant risk factor for restenosis on univariable analysis. There are limited data investigating predictors of decannulation failure after tracheostomy. However, Fiz et al. demonstrated that airway comorbidities (asthma, COPD, unilateral vocal cord paralysis), postoperative complications, and length of resection are risk factors for retreatment.<sup>5</sup> We also demonstrated that postoperative minor complications were associated with both restenosis and permanent tracheostomy. However, we did not demonstrate that length of resection was a risk factor for restenosis or permanent tracheostomy. Postoperative complications may cause wound-healing issues that disrupt maintenance of the repair.

A history of airway trauma was significant on univariable analysis in predicting the likelihood of permanent tracheostomy. Patients with a history of airway trauma may have more cartilaginous and soft tissue damage, which can make the reconstruction more challenging and the healing process more tenuous. Need for repeat surgery was associated with permanent tracheostomy and restenosis on univariable analysis. Stenosis beginning at the level of the vocal cords was associated with permanent tracheostomy. Similarly, combined glottic/subglottic stenosis was associated with a higher risk of permanent tracheostomy. In pediatric patients, Monnier also demonstrated that glottic involvement was associated with less favorable outcomes.<sup>6</sup> Monnier also demonstrated that severe stenosis and comorbidities were associated with a less favorable outcome.

The surgical steps when performing CTR  $\pm$  laryngofissure and TTA have been detailed previously.<sup>1,17</sup> The key features of this technique include minimal posterolateral dissection of the trachea to preserve an adequate vascular supply. Adequate mobilization anterior to the trachea can be safely carried out with blunt dissection to the level of the aortic arch in most patients. This allows a tension-free repair in the majority of cases. We do not perform a laryngeal release, as we feel that this can lead to significant problems with dysphagia, which in some patients may be permanent. Our experience has shown that with the current approach we are able to safely resect up to 5 cm of trachea without any significant problems. This is more than adequate because the majority of lesions in our series required approximately 3 cm of airway resection (range, 1–5 cm). Additionally, neither length of resection or length of stenosis was associated with permanent tracheostomy or restenosis.

We prefer to stent the upper airway in all patients undergoing CTR. The aim of this is to maintain the repair and allow unimpeded healing without restenosis. There are a number of options available. On occasion we have used solid intralaryngeal stents covered with a distal tracheostomy.

However, we prefer using a soft, Silastic T tube, which allows normal respiration and phonation. In addition, the T tube permits occasional toilet of the lower airway. The majority of patients experience some degree of temporary aspiration, which settles with conservative management. We aim to remove the T tube at 6 to 8 weeks postoperatively; however, the precise time required is controversial and still debated in the literature. In this study, longer T-tube duration was associated with a higher risk of permanent tracheostomy. Patients with extensive subglottic stenosis, combined glottic/subglottic stenosis, or significant comorbidities in our experience require a prolonged period of airway stenting. It is possible that the duration of T-tube stenting acts as a surrogate marker for these factors in determining outcome after CTR rather than stenting actually leading to an increased failure rate.

CTR and TTA are complex procedures that are not without risks. We experienced complications (major = 16, minor = 20) in 36 patients. The majority of these were easily managed and reversible. Development of complications was a significant predictor of permanent tracheostomy and restenosis in this study. Restenosis requiring further management occurred in 15 (13%) patients. Ultimately, we were unable to decannulate six (5%) patients after either primary CTR or salvage surgery.

The major limitation of this study is the small sample size. First of all, the sample size of restenosis and permanent tracheostomy is small. Given this, we were not able to do statistical analysis with sufficient power on each variable of interest. For example, we could not do analysis of comorbidity or degree of stenosis in the permanent tracheostomy group. Although history of trauma was a significant predictor of permanent tracheostomy, only seven (6%) patients had airway trauma in this cohort, which limits the analysis. We were able to overcome some of these limitations by combining groups. We created a composite cohort of patients with restenosis and permanent tracheostomy that could allow us to do statistical analysis. Only five patients had grade 4 stenosis, which limits effective analysis. Thus, we combined grade 3 and 4 stenosis in the univariable analysis.

Alternative outcome measures were not included in this retrospective analysis but are equally vital in measuring the success of the management of subglottic stenosis, including physiologic measures of airway resistance (i.e., flow volume loops, body plethysmography), voice analysis, and quality-of-life measures. It is our belief that voice outcomes are good in the majority of patients given the debilitating nature of chronic airway obstruction. The majority of patients undergo significant frame-shift with respect to voice quality, where the ability to carry out activities of daily living without any airway limitation takes on greater importance when compared to obtaining a normal voice. This in part explains our clinical observations; however, prospective quality-of-life measures, using both general and specific instruments (i.e., 36-item Short Form Health Survey and Voice Handicap Index) addressing this issue are needed to confirm this.<sup>18</sup> Future research activity needs to focus on the underlying physiological and molecular factors that predispose some patients to the development of clinically significant upper airway stenosis.

## CONCLUSION

Subglottic stenosis is a heterogeneous and complex clinical entity that provides significant challenges for both the patient and the treating physician. A number of management strategies have been reported in the literature; however, there does not currently exist a uniform approach to this complex problem. We present our experience with CTR and TTA and identified a number of adverse prognostic factors predicting the need for a permanent tracheostomy. Traumatic stenosis, longer T-tube duration, combined glottic/subglottic stenosis, start of stenosis at the vocal cords, postoperative minor complications, and need for repeat surgery were associated with an increased risk of requiring permanent tracheostomy. In summary, 108 patients (95%) were successfully decannulated after undergoing CTR and TTA. Our permanent tracheostomy rate of 5% confirms other publications reporting the excellent outcome achieved with this technique for the definitive management of subglottic stenosis. CTR with or without laryngofissure is our standard of care in patients with subglottic stenosis.

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